PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference STI-PCT2	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US04/39735	International filing date *(day/month/year)* 26 November 2004 (26.11.2004)	Priority date *(day/month/year)* 26 November 2003 (26.11.2003)
International Patent Classification (IPC) or national classification and IPC IPC(7): G01N 29/00, 29/18 and US Cl.: 73/1.02, 1.03, 32a, 61.75, 597, 645-648; 422/68.1, 102		
Applicant SEPARATION TECHNOLOGY, INC.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 7 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____ , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☒ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24 june 2005	10 January 2006 (10.01.2006)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Lydia Dent for Hezron Williams Telephone No. 703-308-7722

Form PCT/IPEA/409 (cover sheet)(April 2005)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/39735

Box No. I Basis of the report

1. With regard to the language, this report is based on:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into English, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4(a))

☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:
pages 1-17,21,23,25,26 and 28-48 as originally filed/furnished
pages* 18-20,22,24 and 27 received by this Authority on 25 August 2005 (25.08.2005)
pages* NONE received by this Authority on _____

☒ the claims:
pages 1-20 as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the drawings:
pages 1/13-5/13 and 7/13-13/13 as originally filed/furnished
pages* 6/13 received by this Authority on 25 August 2005 (25.08.2005)
pages* NONE received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages_____
☐ the claims, Nos_____
☐ the drawings, sheets/figs_____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*):_____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages_____
☐ the claims, Nos_____
☐ the drawings, sheets/figs_____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*):_____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/39735

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-20	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 1-20	YES
	Claims NONE	NO
Industrial Applicability (IA)	Claims 1-20	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)

Claims 1-10 and 18-20 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a system for determining hematocrit or hemoglobin concentration of blood with an analyzer for receiving a sampling device for collecting blood, with an ultrasonic transducer oriented toward an aperture in the sampling device for emitting an ultrasonic signal into the blood sample while still inside the sampling device.

Claims 11-16 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest an apparatus for determining hematocrit or hemoglobin concentration of blood by ultrasonic analysis that includes a sampling device for acquiring a blood sample having a finer-grip at one end and an opposing functional end that includes a collecting region for collecting by capillary action, and a testing region, and a pumping region.

Claim 17 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a blood analysis device for ultrasonically analyzing blood including a disposable blood sampling device that collects a sample by capillary action, and means for transferring the blood to a testing cell by pressure differential.

Claims 1-20 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry.

---------- NEW CITATIONS ----------

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The drawings are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or content thereof: #22 is used for two different elements (#22 is found in Figs. 1, 11, 13 and 14 for one element, and in Figs. 6-9 for another element). #29 does not appear in the drawings where they replaced #22 in the description, or in Figure 11, as indicated in page 24, line14 to page 25, line 8.

Figure 8(d), as mentioned on page 25, line 7, is not in the drawings.

In Fig. 11, #30 does not appear (from page 24, line 23, as amended). There is no #11 shown in Fig. 11.

The description is objected to as containing the following defect(s) under PCT Rule 66.2(a)(iii) in the form or contents thereof: On page 23, lines 8 and 11, #326 should be #325, each occurrence, according to the drawings and to be consistent with page 22, line 20.

cross-section as shown, or oval or various rectilinear shapes. It has been found that a non-circular cross-section such as a star or rectangle augments the capillary draw of the tube 11, but may be more difficult to mold. The entrance aperture of capillary tube 11 protrudes outward for easier collection. Capillary tube 11 continues into a testing region 20 (see below). The walls of the capillary tube 11 are relatively clear or translucent and may be demarcated by visible indicator lines, graduated markings or some other obvious feature to indicate to the user that enough blood has been acquired. In practice, a patient's blood will be drawn by a pin prick (as described below), the entrance aperture of capillary tube 11 will be placed in contact with the blood, and the blood will be inducted by capillary action into the tube 11 until a sufficient quantity is collected. Once done, the capillary tube 11 serves as the temporary storage receptacle for the blood during transit from the patient to the analyzer 10.

The enlarged illustration to the right of FIG. 9 illustrates the connection between the opposing end of tube 11 and testing region 20 of the disposable device 12. The testing region 20 is an open window formed by a transverse aperture 21 through the front and back of the supporting frame of the sampling device 12. Preferably, the aperture 21 is cylindrical to define a round-walled testing channel 25 with cylindrical cross-section. Square or rectangular cross sections are also suitable, but a cylindrical shape (round aperture with flat sides) deters air bubbles from forming in the testing channel 25, while also minimizing the amount of blood required for accurate testing. Two rims surround the aperture 21 on both the front and back surfaces, and these are slightly raised to form sealing rings 29 (see FIG. 8) against the walls of the analyzer 10. The sealing rings 29 form the contact points with the sampling device 12 when it is inserted into the analyzer 10 and the door 20 is latched shut to lock the sampling device 12 in place. Disposable device 12 is squeezed tightly between two walls of the sampling chamber

inside the analyzer 10, said walls mating with the sealing rings 29 to hermetically seal off the testing channel 25. The volume of the sealed testing channel 25 may range from .01 to 1 ml.

The passage of the capillary tube 11 traverses the testing channel 25 at two holes 23, 24 located opposite each other. The far hole 24 continues into the actuator region 30 via a hollow actuator tube 31. As shown in FIG. 6, the actuator tube 31 leads to an actuator orifice 32 that is open through the front of the sampling device 12. Orifice 32 seals over a connection to a small micro-pump (described below) in analyzer 10 that, when activated, draws the blood sample from capillary tube 11 into the sealed testing channel 25.

The capillary tube 11 is vertically-oriented, a substantially vertical orientation of the device 12 is maintained while in the analyzer 10 so that any entrapped air bubbles will migrate up the capillary tube 11 through the testing channel 25 and out the orifice 32.

The actuator tube 31, including ends 34 and 35, is integrally molded (or attached and sealed) at end 34 to the edges of hole 24 of testing channel 25, and this may be accomplished by molding and welding two half-sections or by unitary molding of the entire device 12. In a similar manner to the raised rims around the testing aperture 21, a raised rim exists around the actuating orifice 32. As the sampling device 12 is inserted into the analyzer 10, this rim forms a seal around a mating hole on the wall of the analyzer (not shown), allowing the micro-pump to communicate with the sampling device 12 and pull the fluid up from the collecting region into the testing region.

The disposable 12 is molded with a pair of crescent-shaped apertures 45 on one side. Crescent-shaped apertures 45 add resiliency and allow a degree of compression between the analyzer 10 housing 30 and door 20, helping to create a positive latching effect and securely seating the device 12 in the analyzer 10.

The grip end 1of the disposable 12 may include one or more raised or textured finger grips or raised text 37 (i.e. ridges or bumps) to help prevent dropping of the device during blood collection and transfer to the analyzer 10.

While the preferred embodiment of the disposable device 12 is made generally of hard rubber with integral rubber sealing rings 29, one skilled in the art will understand that the device 12 may be formed substantially of hard plastic with separate rubber grommet-type sealing rings 29. Other possible materials include glass, polystyrene, polyamide, polyvinylchloride, polycarbonate, silicone, polypropylene, polyurethane, latex or polyethylene. The choice of materials and surface finishes for the device12 are preferably chosen to prolong the onset of coagulation (i.e. Pebax is suitable). This is particularly desirable when using untreated capillary blood in an ultrasonic analyzer because it has been demonstrated that the biochemical process of coagulation changes the speed of sound over time. Surface finishes are preferably smooth to minimize the surface area, allowing the blood to flow more freely through the device and prolong the onset of coagulation.

The sampling device 12 may be manufactured by one-shot molding, or two-shot molding in separate halves that are then hot-welded together, the sealing rings 29 and other flexible components being integrally molded or added separately. The various parts may be connected by snaps, adhesive, ultrasonic welding, or any other method of securing differing plastic or rubber materials. The sampling device 12 may also be formed using blow molding.

The sampling device 12 will function with a drop of venous blood, but more preferably it is optimized for application with capillary blood. Capillary blood tends to have a slightly different mixture of components than venous or arterial blood. For example, the HCT and HGB of sampled capillary blood is typically 2- 5 % higher than a sample taken from the vein, a

heparin anticoagulant, EDTA or other anticoagulants, may be coated inside the device to retard coagulation without distorting red blood cells.

The frame structure of the disposable device 12 is specifically designed to mate with port 22 of the analyzer 10 (See Figures 1 and 2), and the port 22 requires certain structure to work with the device 12. The port 22 structure includes the door 20 hinged to the main housing 30 of the analyzer 10 and closing and latching shut to capture and seat the sampling device 12 inside with one or more sensors 227 directed orthogonally through (and sealing off) the test cell 25 of the disposable 12 as shown in FIG. 9. Thus, the disposable device 12 is inserted into port 22 with blood sample already in the capillary tube 11.

While the embodiment of FIGs. 6-9 relies on a micro-pump engaged to the disposable 12 orifice, FIG. 10 is a composite drawing showing an alternative disposable embodiment 300 in which the action of the micro-pump in analyzer 10 is replaced by an on-board actuator bulb 332 on the disposable 300. The actuator bulb 332 is preferably made of flexible rubber or plastic and may be integrally molded in the sampling device 300 (by molding and welding two half-sections or by unitary molding of the device 300). The actuator bulb 332 is sealed and feeds a pressure differential through a connected actuator tube 331 into testing chamber 325. The actuator bulb 332 protrudes above the plane of the device 300, and the port 22 is formed with constricted sides (or protrusions) at a predetermined depth. Thus, as device 300 is inserted, the sides of the port 301 depress the actuator bulb 332 forcing air through actuator tube 331 into testing cylinder 325, and then releases the bulb 332 as the bulb travels past. This way, when the device 300 is inserted into port 301 with blood sample already in the capillary tube 11, the walls of the sample chamber 22 squeeze and release the bulb 332. As before, sealing rings 322 around the test chamber 325 act as a wiping mechanism against the sensor housing surfaces 328 (which contain one or more

Further, the sampling device and sample chamber may comprise a tubular arrangement such that the blood is collected from the patient using a venipuncture needle or other needle device, whereupon the blood flows through a length of tubing. The length of tubing can act as the sample chamber, particularly for the attenuation coefficient and speed of sound measurement methods performed on a sample flowing through the length of tubing. In any event, a calibration can be obtained using samples of independently measured hematocrit, permitting the measurement of the HCT, MCV and/or RBC of the sample, even when flowing through the sample chamber.

Sample Chamber 22 and Transducer(s) 227

FIG. 11 is a side cross-section illustrating the fit of the disposable sampling device 12 in the sampling chamber 22 of analyzer 10, and FIG. 12 is an operational schematic. The port 22 contains one or more transducers 227 having raised sensing surfaces 228 that engage the sealing rings 29 of device 12, the sealing rings 29 acting as a wiping mechanism, cleaning the parallel sensing surfaces 228 of the sensors 227 within the analyzer 10. When fully inserted, the disposable 12 bottoms out in door 20 guaranteeing that the disposable 12 is located correctly with respect to the sensing surfaces 228. The sealing rings 29 then form a hermetic seal against the sensing surfaces 228, thereby forming a closed test cell 25. FIG. 11 illustrates the final position of the disposable 12 with micropump 210 facing the actuator region 30 and raised sensing surfaces 228 around sensor 227 engaged with the sealing rings 29 so that the sensor 227 communicates with the testing channel 25. Micro-pump 210 may be any of a variety of commercially-available micro-pumps such sold by Micropump, Inc., such as their leak-free sealless magnetic drive low flow pumps for metering and dosing liquids.

inferred by measuring the speed of sound through the walls. The temperature may also be controlled so that no temperature variations affect the measurement. The preferred embodiment employs measurement using a temperature sensing device 90 such as a thermistor. For example, thermistor 90 is included on the other side of sample chamber 22 for sensing the temperature of the blood sample in sampling device 12. Preferably, the thermistor 90 is mounted on the inner surface of the chamber so that it can measure the blood temperature by direct contact. If this presents cleaning or contamination problems, another preferable embodiment is to embed the thermistor directly behind the wall of the chamber 90. Measuring the temperature of the metal gap of sample chamber 22 also allows the device to compensate for thermal expansion. The transducers 227 and thermistor 90 are electrically connected to the circuit board internal to analyzer 10.

Once the analysis is complete, micro-pump 210 exerts a small amount of reverse pressure to force the blood out of the testing cell 25 and back into capillary tube 11. As the device 12 is removed from the analyzer 10, the sealing rings 29 again serve as a wiping mechanism, cleaning off the sensing surfaces 228. The danger of inadvertent exposure to the blood is eliminated by the sequential use of capillary action and pressure-differential to move the blood from containment, to sample chamber, and back, automatically upon insertion and withdrawal.

FIG. 13 is a side perspective view of the analyzer 10 with snap-in door 20 removed from its hinges to illustrate insertion of the sampling device 12 into sample chamber 22. The sample chamber 22 maintains precise alignment of the various components, especially the alignment between transducer(s) and the sampling device 12. The walls 62 of sample chamber 22 are formed of a material chosen for structural strength. Preferred sample chamber 22 materials include steel or brass. The chamber 22 is preferably manufactured to precisely known

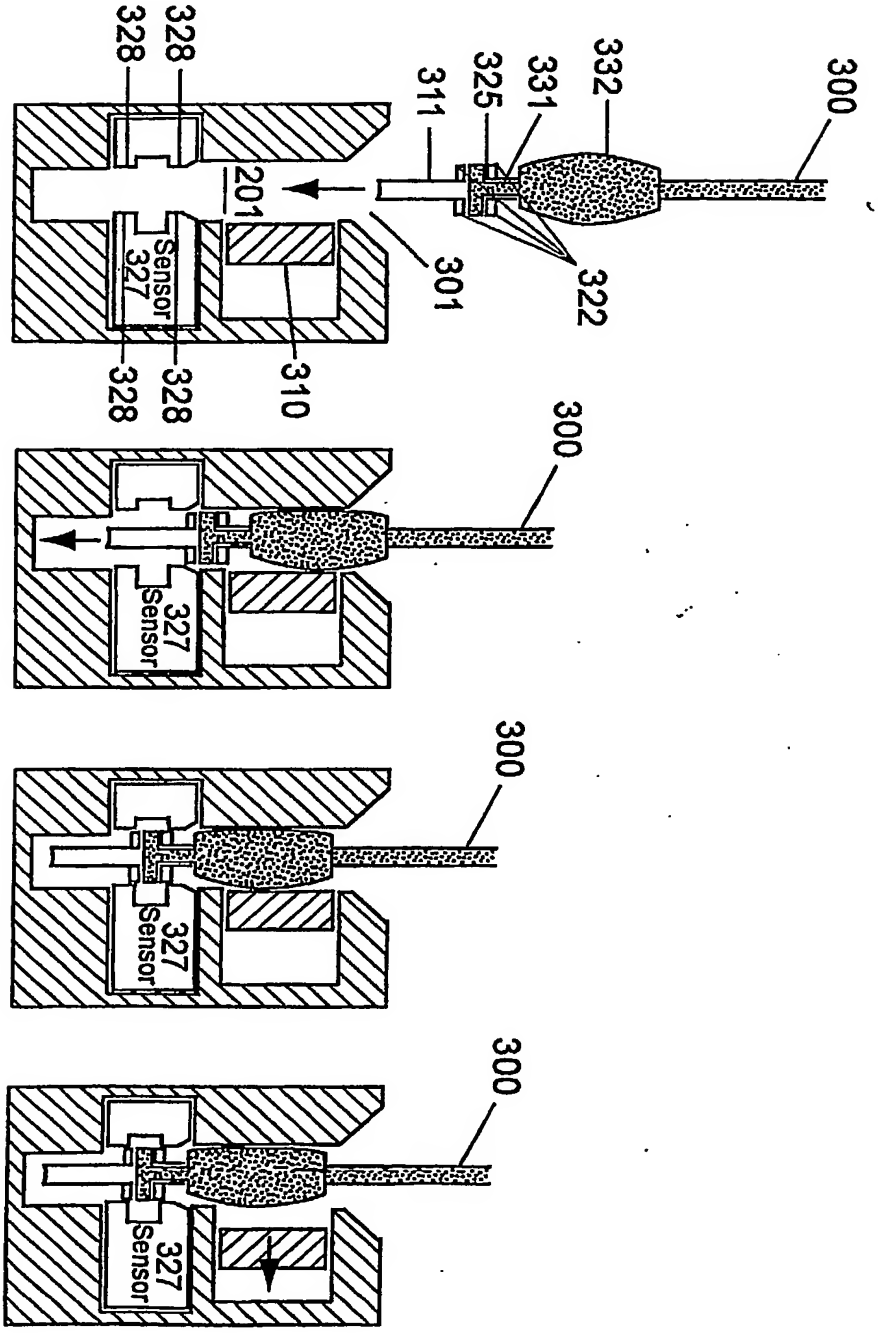

FIG. 10

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